☐ an Independent Inventor

☐ a Small Business Concern

☐ a Nonprofit Organization

☐ This application is no longer entitled to small entity status. It is requested that this be noted in the files of the Patent and Trademark Office.

☐ Substitute Pages _____ of the Specification are enclosed.

☐ An Abstract is enclosed.

☐ _____ Sheets of Proposed Corrected Drawings are enclosed.

☐ A Certified Copy of each of the following applications: _____ _____ is enclosed.

☐ An Associate Power of Attorney is enclosed.

☐ Information Disclosure Statement.

☐ Attached Form 1449.

☐ A copy of each reference as listed on the attached Form PTO-1449 is enclosed herewith.

☐ Appended Material as follows: _____ .

☐ Other Material as follows: _____ .

FEE CALCULATION

☐ No Additional Fee is Due.

				SMALL ENTITY		NOT SMALL ENTITY	
	REMAINING AFTER AMENDMENT	HIGHEST PAID FOR	EXTRA	RATE	FEE	RATE	FEE
TOTAL CLAIMS	72	72 (20 MINIMUM)	0	$9 EACH	$0.00	$18 EACH	$
INDEP. CLAIMS	7	7 (3 MINIMUM)	0	$42 EACH	$0.00	$84 EACH	$
FIRST PRESENTATION OF MULTIPLE DEPENDENT				$140	$	$280	$
☐ ONE MONTH EXTENSION OF TIME				$55	$	$110	$
☒ TWO MONTH EXTENSION OF TIME				$200	$200	$400	$
☐ THREE MONTH EXTENSION OF TIME				$460	$	$920	$
☐ FOUR MONTH EXTENSION OF TIME				$720	$	$1440	$
☐ FIVE MONTH EXTENSION OF TIME				$980	$	$1960	$
☐ LESS ANY EXTENSION FEE ALREADY PAID				minus	($)	minus	($)
☐ TERMINAL DISCLAIMER				$55	$	$110	$
☐ OTHER FEE OR SURCHARGE AS FOLLOWS:							
TOTAL FEE DUE					$200.00		$

☒ A Check is Enclosed in the Foregoing Amount Due.

☒ Petition is hereby made under 37 C.F.R. 1.136(a) to extend the time for response to the Office Action of **January 17, 2002** to and through **April 17, 2002** comprising an extension of the shortened statutory period of **two (2)** month(s).

☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is

further authorized to charge any fees related to any such extension of time to deposit account 23-3050. This sheet is provided in duplicate.

☒ The Commissioner is authorized to charge payment of the following fees and to refund any overpayment associated with this communication or during the pendency of this application to deposit account 23-3050. This sheet is provided in duplicate.

☐ The Foregoing Amount Due for Filing this Paper.

☒ Any additional filing fees required, including fees for the presentation of extra claims under 37 C.F.R. 1.16.

☒ Any additional patent application processing fees under 37 C.F.R. 1.17 or 1.20(d).

SHOULD ANY DEFICIENCIES APPEAR with respect to this application, including deficiencies in payment of fees, missing parts of the application or otherwise, the United States Patent and Trademark Office is respectfully requested to promptly notify the undersigned.

Date: Apr 16 2002

Patrick J. Farley
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Nicholas C. Nicolaides, et al.

Serial No.: 09/707,468 Group Art Unit: 1633

Filing Date: November 7, 2000 Examiner: D. Nguyen

For: METHODS FOR GENERATING GENETICALLY ALTERED ANTIBODY-PRODUCING CELL LINES WITH IMPROVED ANTIBODY-CHARACTERISTICS

DATE OF DEPOSIT: **April 16, 2002**
EXPRESS MAIL NO: **EL 884784412 US**

Assistant Commissioner for Patents
Washington DC 20231

Dear Sir:

RESPONSE TO REQUIREMENT FOR RESTRICTION UNDER 37 C.F.R. § 1.143

This is in response to the Office Action dated January 17, 2002. A petition for a two-month extension of time is included herewith.

The Examiner has set forth twenty-five Groups of claims and has required the election of one Group for examination. Applicants hereby traverse. However, in order to be fully responsive to the Office Action, Applicants hereby elect Group I (Claims 1-4, 9-11, 22-25, and 29).

The Examiner alleges that an "enormous" number of distinct inventions are claimed, and that it would be unduly burdensome to search and/or consider the patentability of the claims that embrace distinct inventions. The Applicants respectfully disagree.

As a preliminary matter, the Examiner has designated two Groups of claims as "Group XVII" and two Groups of claims as "Group XVIII." The second Group XVII,

which appears in the Office Action on page 6, and the second Group XVIII, which appears on page 7, are believed to be inadvertent entries, which are apparently unrelated to this Application. Applicants respectfully request withdrawal of these additional groups, which will not be addressed further in this response.

Groups I, II, III, IV, and VIII are all drawn to methods for the making of a hypermutated antigen comprising a dominant negative allele of a mismatch repair gene, as claimed generically in Claim 1. As noted by the Examiner each of these Groups is classified in Class 435, subclasses 325 and 455, and Class 514, subclass 44. It would therefore, not be unduly burdensome for the Examiner to consider the patentability of the claims in Groups I, II III, IV, and VIII as these groups share common Classifications.

Furthermore, the dependent claims set forth the dominant negative mismatch repair genes that may be used in the methods of the invention. The Specification further sets forth the nucleotide sequences and the encoded amino acid sequences of the mismatch repair genes. We invite the Examiner's attention to the MPEP, 8th edition, Section 803.04 wherein it is stated:

> "It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application ***without restriction***." (emphasis added)

The Commissioner instituted a policy *sua sponte* to aid the biotechnology industry without placing an undue burden on the Examiners. The policy essentially waives the normal requirements relating to independent and distinct inventions. Without conceding that the groups represent independent and distinct inventions, it is submitted that since Groups I, II, III, IV, and VIII drawn only *six* mismatch repair genes, albeit not expressly by a sequence identification number, this would not cause an undue burden to be placed upon the Examiner as the Specification provides sequences of the mismatch repair genes. Applicants respectfully request that Groups I-IV and VIII be joined as a single Group, which if joined, would be elected for examination in this application.

Claims in Groups V, VI, and VII are drawn to methods for the making of a transgenic animal. Groups V, VI, VII are classified in Class 800, subclass 25. Thus, it would not be unduly burdensome for the Examiner to search examine these three groups in a single application. Furthermore, the dependent claims set forth the

dominant negative mismatch repair genes that may be used in the methods of the invention. The Specification further sets forth the nucleotide sequences and the encoded amino acid sequences of the mismatch repair genes. As discussed above, it is a policy instituted by the Commissioner that up to ten independent and distinct sequences may be examined in the same application without a requirement for restriction. Therefore, Applicants respectfully request that Groups V, VI and VII be joined into a single Group. Furthermore, as Groups V, VI, and VII are linked by Claim 1, Applicants request that upon allowance of the linking claim, that the unified Group be rejoined to the elected group.

Claims in Groups IX, X, XI, XII are drawn to methods for generating a mutation in a gene affecting antibody production in an antibody-producing cell, which comprises growing the cell and testing the cell to determine if the gene harbors a mutation. The four groups are related in that they involve a determination of an effect on antibody production. The Examiner restricts the claims based on methods of testing; the methods of testing involve analysis of nucleic acid sequences, proteins, phenotype and binding activity of antibodies. As there are only 4 types of testing to be searched, there is not an undue burden on the Examiner to examine these claims in a single application. Applicant respectfully requests that Groups IX, X, XI, XII be joined in a single Group.

Additionally, as noted by the Examiner Groups X and XII are classified in class 435, subclass 7.1. It would therefore, not be unduly burdensome for the Examiner to consider the patentability of the claims in Groups X and XII together as these groups share common classifications. If the Examiner will not join Groups IX, X, XI, XII, Applicants respectfully request that the examiner consider joining Groups X and XII into one Group.

Groups XIII and XIV, both of which encompass claims 36-41, are related and the restriction is not proper. The Examiner states that Group XIII is drawn to *in vitro* methods of testing and Group XIV is drawn to *in vivo* methods of testing. This is not correct. Claims 36-41 do not set forth such limitations. Therefore, claims 36-41 should not be separated into two Groups covering *in vitro* or *in vivo* methods of testing. The Applicants respectfully request that Groups XIII and XIV be joined into a single Group.

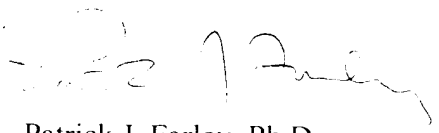
Groups XV and XVI are related and the restriction requirement is not proper. The Examiner states that Group XV is drawn to *in vitro* methods of testing a cell and

Group XVI is drawn to *in vivo* methods of testing a cell. However, the claims that comprise Groups XV and XVI do not set forth such limitations. Therefore, the restriction requirement is improper and the Applicants respectfully request that Groups XV and XVI be joined into a single group. Groups XVII, XVIII, and XIX are alleged to claim distinct inventions. The Applicants respectfully disagree and request that this restriction be withdrawn. As noted by the Examiner each of these Groups is classified in class 514, subclass 44. It would therefore, not be unduly burdensome for the Examiner to consider the patentability of the claims in Groups XVII, XVIII, and XIX as these groups share common classifications. In addition, these Groups differ with respect to the mismatch repair gene claimed, albeit not by express sequence identification numbers. As discussed above, however, the Specification sets forth the nucleotide sequences and the encoded amino acid sequences of the mismatch repair genes. As discussed above, it is a policy instituted by the Commissioner that up to ten independent and distinct sequences may be examined in the same application without a restriction requirement. Pursuant to the spirit of the policy instituted by the Commissioner regarding biotechnology inventions, Applicants believe that the claims in Groups XVII, XVIII, and XIX may be examined in the same application without placing an undue burden on the Examiner. Therefore, Applicants respectfully request that Groups XVII, XVIII, and XIX be joined into a single Group.

Groups XX, XXI, XXII, and XXIII are alleged to claim distinct inventions. The Applicants respectfully disagree and request that this restriction be withdrawn. As noted by the Examiner each of these Groups is classified in class 424, subclass 130.1. It would therefore, not be unduly burdensome for the Examiner to consider the patentability of the claims in Groups XX, XXI, XXII, and XXIII as these groups share common classifications. In addition, these Groups differ with respect to the mismatch repair gene claimed. As discussed above the Specification sets forth the nucleotide sequences and the encoded amino acid sequences of the mismatch repair genes. As discussed above, it is a policy instituted by the Commissioner that up to ten independent and distinct sequences may be examined in the same application without a restriction requirement. Pursuant to this policy instituted by the Commissioner regarding biotechnology inventions, Applicants believe that the claims in Groups XX, XXI, XXII, and XXIII may be examined in the same application without placing an

undue burden on the Examiner. Therefore, Applicants respectfully request that Groups XX, XXI, XXII, and XXIII be joined into a single Group.

Respectfully submitted,



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April 16, 2002

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